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FILE COVERS 1907 - 18 Jul 2008 VOL 149 ISS 4
FILE LAST UPDATED: 17 Jul 2008 (20080717/ED)

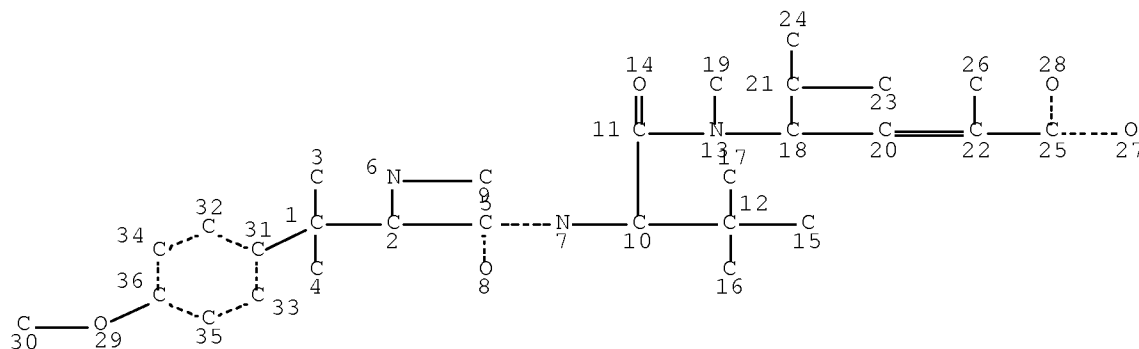
Caplus now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2008.

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<http://www.cas.org/legal/infopolicy.html>

=> d que l12

L10 STR



NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 36

STEREO ATTRIBUTES: NONE

L11 2 SEA FILE=REGISTRY FAM FUL L10

L12 2 SEA FILE=CAPLUS ABB=ON PLU=ON L11

=> fil wpix

FILE 'WPIX' ENTERED AT 17:32:48 ON 18 JUL 2008

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FILE LAST UPDATED: 15 JUL 2008 <20080715/UP>

MOST RECENT THOMSON SCIENTIFIC UPDATE: 200845 <200845/DW>

DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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>>> IPC Reform backfile reclassifications have been loaded to the end of March 2008. No update date (UP) has been created for the reclassified documents, but they can be identified by 20060101/UPIC and 20061231/UPIC, 20070601/UPIC, 20071001/UPIC, 20071130/UPIC and 20080401/UPIC. ECLA reclassifications to April and US national classifications to the end of January 2008 have also been loaded. Update dates 20080401/UPEC and /UPNC have been assigned to these. <<<

FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE, PLEASE VISIT:

http://www.stn-international.de/training_center/patents/stn_guide.pdf

FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE

<http://scientific.thomsonreuters.com/support/patents/coverage/latestupdates/>

EXPLORE DERWENT WORLD PATENTS INDEX IN STN ANAVIST, VERSION 2.0:

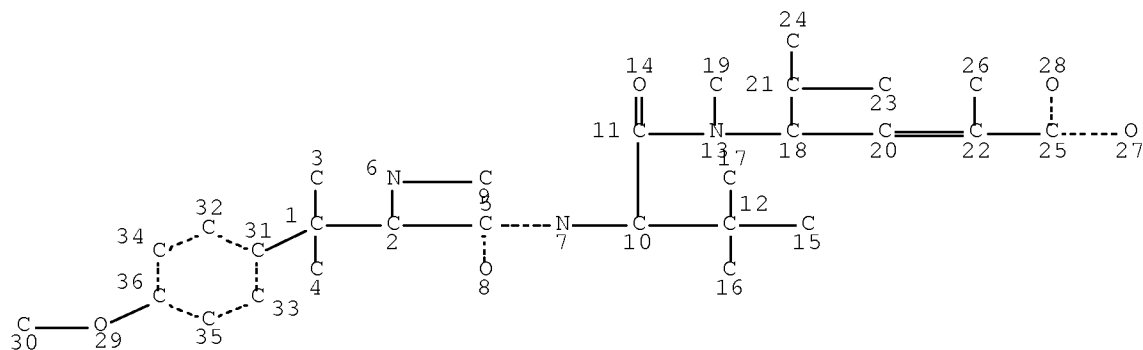
http://www.stn-international.com/archive/presentations/DWPIAnaVist2_0710.pdf

>>> HELP for European Patent Classifications see HELP ECLA, HELP ICO <<<

>>> Please note that the COPYRIGHT notification has changed <<<

=> d que 122

L10 STR



NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 36

STEREO ATTRIBUTES: NONE

L20 4 SEA FILE=WPIX SSS FUL L10

L21 4 SEA FILE=WPIX ABB=ON PLU=ON L20/DCR

L22 4 SEA FILE=WPIX ABB=ON PLU=ON L21 AND (?PACLIT? OR ?TUMOR? OR ?TUMOUR? OR ?CHEMOTHER? OR ?MICROTUB? OR ?OVAR?)

=> dup rem 112 122

FILE 'CAPLUS' ENTERED AT 17:32:53 ON 18 JUL 2008
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 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE 'WPIX' ENTERED AT 17:32:53 ON 18 JUL 2008
 COPYRIGHT (C) 2008 THOMSON REUTERS
 PROCESSING COMPLETED FOR L12
 PROCESSING COMPLETED FOR L22
 L23 5 DUP REM L12 L22 (1 DUPLICATE REMOVED)
 ANSWERS '1-2' FROM FILE CAPLUS
 ANSWERS '3-5' FROM FILE WPIX

=> d 123 ibib abs hitind hitstr 1-2; d 123 ibib abs hitstr 3-5

L23 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 1
 ACCESSION NUMBER: 2004:267231 CAPLUS Full-text
 DOCUMENT NUMBER: 140:304081
 TITLE: Preparation of peptides for treating resistant tumors
 INVENTOR(S): Greenberger, Lee Martin; Loganzo, Frank, Jr.;
 Discafani-Marro, Carolyn Mary; Zask, Arie;
 Ayrall-Kaloustian, Semiramis
 PATENT ASSIGNEE(S): Wyeth Holdings Corporation, USA
 SOURCE: PCT Int. Appl., 442 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026293	A2	20040401	WO 2003-US29832	20030918
WO 2004026293	A3	20041216		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2406504	A1	20040320	CA 2002-2406504	20021003
AU 2003275126	A1	20040408	AU 2003-275126	20030918
US 20040121965	A1	20040624	US 2003-666722	20030918
PRIORITY APPLN. INFO.:			US 2002-411883P	P 20020920
			WO 2003-US29832	W 20030918

OTHER SOURCE(S): MARPAT 140:304081

AB The invention provides peptides R1R2NCH(CR3R4R5)CONR6CHR7CONR8R9 [R1-R8 are H or an (un)saturated moiety having a linear, branched, or cyclic skeleton containing 1-10 (un)substituted carbon atoms and 0-4 each nitrogen, oxygen, or sulfur atoms; or R1R2N or R3R4C is a 3- to 7-membered ring; R9 is -Y-CO-Z, where Y is alkyl and Z is OH, SH, NH2, an amino acid residue, etc. (with provisos)] for treating or inhibiting the growth or eradication of tumors which are resistant to at least one chemotherapeutic agent. Thus, N,β,β-trimethyl-L-phenylalanyl-N1-[(1S,2E)-3-carboxy-1- isopropylbut-2-enyl]-N1,3-dimethyl-L-valinamide was prepared and shown to be a potent inhibitor of cell growth in 34 tumor cell lines (mean IC50 = 2.1 ± 1.7 nM, median 1.7 nM, range

0.2-7.3 nM) and is distinct from paclitaxel which has an usually large range of activity. The activity is independent of tumor origin and in many cases this peptide is considerably more potent than paclitaxel.

IC ICM A61K031-191

ICS A61K031-194; A61P035-00; A61K031-192; A61K031-195

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1

IT 169181-24-2P 228266-42-0P 228266-48-6P 228266-49-7P 500229-47-0P
 676631-37-1P 676631-40-6P 676631-42-8P 676631-44-0P 676631-47-3P
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of peptides for treating resistant tumors)

IT ~~676633-18-4P~~ ~~676633-19-5P~~

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

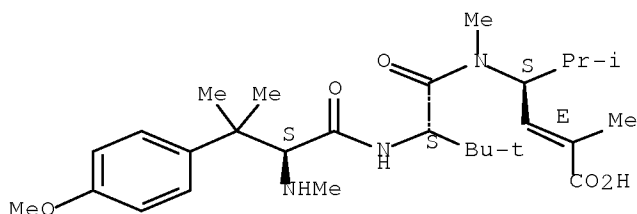
(preparation of peptides for treating resistant tumors)

RN 676633-18-4 CAPLUS

CN L-Valinamide, N,O, β , β -tetramethyl-L-tyrosyl-N-[(1S,2E)-3-carboxy-1-(1-methylethyl)-2-butenyl]-N,3-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



RN 676633-19-5 CAPLUS

CN L-Valinamide, N,O, β , β -tetramethyl-L-tyrosyl-N-[(1S,2E)-3-carboxy-1-(1-methylethyl)-2-butenyl]-N,3-dimethyl-, mono(trifluoroacetate) (9CI)
(CA INDEX NAME)

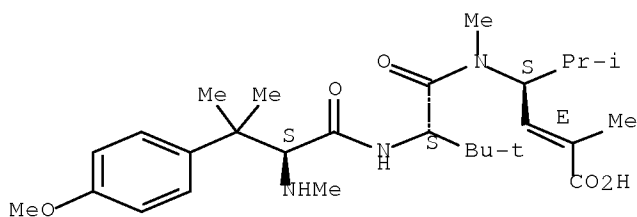
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CRN 676633-18-4

CMF C28 H45 N3 O5

Absolute stereochemistry.

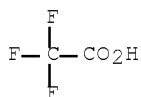
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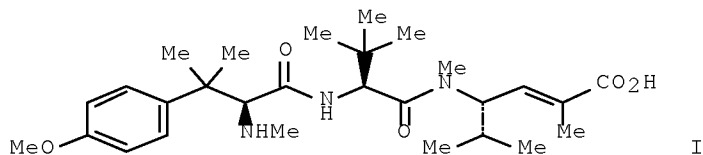
CM 2

CRN 76-05-1

CMF C2 H F3 O2



L23 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2004:617803 CAPLUS Full-text
 DOCUMENT NUMBER: 141:314607
 TITLE: Synthesis and Biological Activity of Analogues of the
 Antimicrotubule Agent N, β , β -Trimethyl-L-
 phenylalanyl-N1-[(1S,2E)-3-carboxy-1-isopropylbut-2-
 enyl]- N1,3-dimethyl-L-valinamide (HTI-286)
 AUTHOR(S): Zask, Arie; Birnberg, Gary; Cheung, Katherine; Kaplan,
 Joshua; Niu, Chuan; Norton, Emily; Suayan, Ronald;
 Yamashita, Ayako; Cole, Derek; Tang, Zhilian;
 Krishnamurthy, Girija; Williamson, Robert; Khafizova,
 Gulnaz; Musto, Sylvia; Hernandez, Richard; Annable,
 Tami; Yang, Xiaoran; Discafani, Carolyn; Beyer, Carl;
 Greenberger, Lee M.; Loganzo, Frank; Ayrat-Kaloustian,
 Semiramis
 CORPORATE SOURCE: Chemical and Screening Sciences, and Oncology
 Research, Wyeth Research, Pearl River, NY, 10965, USA
 SOURCE: Journal of Medicinal Chemistry (2004), 47(19),
 4774-4786
 CODEN: JMCMAR; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 141:314607
 GI



AB Hemiasterlin, a tripeptide isolated from marine sponges, induces microtubule depolymn. and mitotic arrest in cells. HTI-286, an analog from an initial study of the hemiasterlins, is presently in clin. trials. In addition to its potent antitumor effects, HTI-286 has the advantage of circumventing the P-glycoprotein-mediated resistance that hampers the efficacy of other antimicrotubule agents such as paclitaxel and vincristine in animal models. This paper describes an in-depth study of the structure-activity relationships (SAR) of analogs of HTI-286, their effects on microtubule polymerization, and their in vitro and in vivo anticancer activity. Regions of the mol. necessary for potent activity are identified. Groups tolerant of modification, leading to novel analogs, are reported. Potent analogs identified through in vivo studies in tumor xenograft models include one superior analog, HTI-042 (I).

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1

IT 228266-43-1P 228266-45-3P 228266-48-6P ~~676633-19-5P~~
 676633-61-7P 676633-65-1P 676633-77-5P 676633-80-0P 676633-90-2P
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL
 (Biological study); PREP (Preparation)

(preparation of analogs of peptide HTI-286 and SAR study of their
 anticancer

activity and effects on microtubule polymerization)

IT ~~676633-19-5P~~

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL
 (Biological study); PREP (Preparation)

(preparation of analogs of peptide HTI-286 and SAR study of their
 anticancer

activity and effects on microtubule polymerization)

RN 676633-19-5 CAPLUS

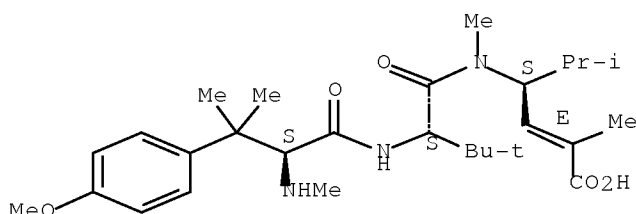
CN L-Valinamide, N,O, β , β -tetramethyl-L-tyrosyl-N-[(1S,2E)-3-carboxy-
 1-(1-methylethyl)-2-butenyl]-N,3-dimethyl-, mono(trifluoroacetate) (9CI)
 (CA INDEX NAME)

CM 1

CRN 676633-18-4

CMF C28 H45 N3 O5

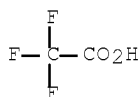
Absolute stereochemistry.
 Double bond geometry as shown.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 3 OF 5 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
 ACCESSION NUMBER: 2005-273356 [28] WPIX
 CROSS REFERENCE: 2003-812505
 DOC. NO. CPI: C2005-085598 [28]
 TITLE: New Hemiasterlin analogs are tumor growth inhibitors useful in the treatment of cancers e.g. prostate, ovarian, breast and colon cancer and proliferative disorders
 DERWENT CLASS: B05
 INVENTOR: CAMPAGNA S A; FANG F G; KOWALCZYK J J; KUZNETSOV G; SCHILLER S; SELETSKY B M; SPYVEE M; YANG H; CAMPAGNA S; FANG F; KOWALCZYK J; SELETSKY B
 PATENT ASSIGNEE: (EISA-C) EISAI CO LTD; (CAMP-I) CAMPAGNA S A; (FANG-I) FANG F G; (KOWA-I) KOWALCZYK J J; (SCHI-I) SCHILLER S; (SELE-I) SELETSKY B M; (SPYV-I) SPYVEE M; (YANG-I) YANG H
 COUNTRY COUNT: 107

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2005030794	A2	20050407	(200528)*	EN	311[0]	
EP 1664088	A2	20060607	(200638)	EN		
AU 2004276261	A1	20050407	(200677)	EN		
KR 2006095992	A	20060905	(200705)	KO		
CN 1886421	A	20061227	(200731)	ZH		
IN 2006KN00835	P2	20070413	(200735)	EN		
JP 2007537136	W	20071220	(200802)	JA	291	
US 20080108820	A1	20080508	(200833)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005030794	A2	WO 2004-US30921	20040922
AU 2004276261	A1	AU 2004-276261	20040922
CN 1886421	A	CN 2004-80033218	20040922
EP 1664088	A2	EP 2004-784686	20040922
EP 1664088	A2	WO 2004-US30921	20040922
KR 2006095992	A	WO 2004-US30921	20040922
IN 2006KN00835	P2	WO 2004-US30921	20040922
JP 2007537136	W	WO 2004-US30921	20040922
JP 2007537136	W	JP 2006-527135	20040922
KR 2006095992	A	KR 2006-705861	20060324
IN 2006KN00835	P2	IN 2006-KN835	20060405
US 20080108820	A1 Provisional	US 2002-366592P	20020322
US 20080108820	A1 CIP of	WO 2003-US8888	20030321
US 20080108820	A1 Cont of	US 2003-667864	20030922
US 20080108820	A1	WO 2004-US30921	20040922
US 20080108820	A1	US 2007-572871	20070522

FILING DETAILS:

PATENT NO	KIND	PATENT NO

EP 1664088	A2	Based on	WO 2005030794	A
AU 2004276261	A1	Based on	WO 2005030794	A
KR 2006095992	A	Based on	WO 2005030794	A
JP 2007537136	W	Based on	WO 2005030794	A
US 20080108820	A1	Cont of	US 7064211	B

PRIORITY APPLN. INFO: US 2003-667864 20030922
 US 2002-366592P 20020322
 WO 2003-US8888 20030321
 US 2007-572871 20070522

AN 2005-273356 [28] WPIX

CR 2003-812505

AB WO 2005030794 A2 UPAB: 20051222

NOVELTY - A hemiasterlin analog or its derivative is new.

DETAILED DESCRIPTION - A hemiasterlin analog of formula R1-N(R2)-(C(R3)(R4))n-X1-N(R5)-CH(R6)-C(O)-N(R7)-R-X2-Q (I) or its derivative is new.

n = 0 - 4;

X1 and X2 = CRaRb, -C(O)- or SO2;

R1 = H, C(O)Rc or (hetero)aliphatic, (hetero)alicyclic or (hetero)aryl;

R2 = R1 or absent;

Rc = H, OH, ORd or (hetero)aliphatic, (hetero)alicyclic or (hetero)aryl;

Rd, Rf and R = (hetero)aliphatic, (hetero)alicyclic or (hetero)aryl;
 two of R1 - R4 taken together = (hetero)alicyclic, alicyclic(aryl), heterocyclic(aryl), alicyclic(heteroaryl), heteroalicyclic(heteroaryl) or (hetero)aryl;

R5 and R6 = H, C(O)Re, (hetero)aliphatic, (hetero)alicyclic or (hetero)aryl;

R7 = R6 or absent;

Re = H, OH, ORf or (hetero)aliphatic, (hetero)alicyclic or (hetero)aryl;

Q = ORq, SRq, NRqRq', N3, =N-OH or (hetero)aliphatic, (hetero)alicyclic or (hetero)aryl;

Ra, Rb, R4 Rq and Rq' = H or an (hetero)aliphatic, (hetero)alicyclic, or (hetero)aryl;

R3 = Ra or absent;

two of R5 - R7 taken together and NRqRq' = (hetero)alicyclic, alicyclic(aryl), heteroalicyclic(aryl), alicyclic(heteroaryl), heteroalicyclic(heteroaryl) or (hetero)aryl;

-R-X2-Q = optionally substituted alkyl or -Q'-C(O)X;

Q' = optionally substituted CH2, CH2CH2, CH2CH2CH2, CH2CH=CH, CH2C=C or phenylene moiety;

X = OR', SR' or NR'Ru;

R' and Ru = H or optionally substituted alkyl.

Provided that:

(1) when NR7 is linked to R via a double bond, R7 is absent;

(2) (I) is not naturally occurring Hemiasterlin; and

(3) the following groups do not occur simultaneously: n is 1; X1 and X2 are C(O); R1 is H or optionally substituted alkyl or acyl or optionally substituted methylene or -CH= group bonded to the indole moiety to form tricyclic moiety; R2 is H, optionally substituted alkyl or acyl or is absent when R1 is CH=; R3 is H or is absent when CR3 and CRyRz are linked by a double bond; R4 is -C(Rz)(Ry)-indol-3-yl (substituted on 1-position by Rw, on 2-position by Rx and on phenyl ring by (Y)m) where Rw, and Ry is H or optionally substituted alkyl or acyl, Rz is Rw or absent when CR3 and CRyRz are linked by a double bond, m is 0 - 4, Rx is H, an optional substituent or absent when R1 is optionally substituted methylene or -CH=, and Y is optional substituent, Ry and Rz are not H simultaneously; R5 is H, OH or optionally substituted alkyl or acyl; R6 is H or optionally substituted alkyl; R7 is H or alkyl.

INDEPENDENT CLAIMS are included for the following:

(1) an intermediate of formula (II) for the preparation of Hemiasterlin derivative of formula (III);

(2) an intermediate of formula (IV) (where R₂ is H or optionally substituted linear or branched, cyclic or acyclic or optionally saturated lower alkyl, heteroalkyl, alkyl(aryl) or acyl, and R₆ is optionally substituted, linear or branched, cyclic or acyclic or optionally saturated lower alkyl) for the preparation of Hemiasterlin derivative of formula (V) (in which R₂ is H or optionally substituted linear or branched, cyclic or acyclic or optionally saturated lower alkyl, heteroalkyl, alkyl(aryl) or acyl and R₆ is optionally substituted, linear or branched, cyclic or acyclic or optionally saturated lower alkyl); and

(3) a pharmaceutical composition comprising (I), a carrier or diluent, and optionally a further additional therapeutic agent.

g = 1 - 4;

L = CRgRh, S, O or NRk;

Rg, Rh, Rk, Rg₁, Rm₁ and Rm₂ = H or (hetero)aliphatic, (hetero)alicyclic or (hetero)aryl;

two adjacent Rg, Rh, Rk, Rg₁, Rm₁ and Rm₂ taken together = optionally substituted (hetero)alicyclic moiety containing 3 - 6 atoms or (heteroaryl) moiety;

R_{10a} = H or linear or branched, cyclic or acyclic, optionally saturated, optionally substituted alkyl.

ACTIVITY - Cytostatic; Vasotropic.

MECHANISM OF ACTION - Tumor cell growth inhibitor.

(I) Were tested for tumor cell growth inhibitory activity using cultured human cancer cells and MDA-MB-435 cell growth inhibitory assay. (I) Showed an IC₅₀ of 0.1 - 10 nM. No results for specific compounds given.

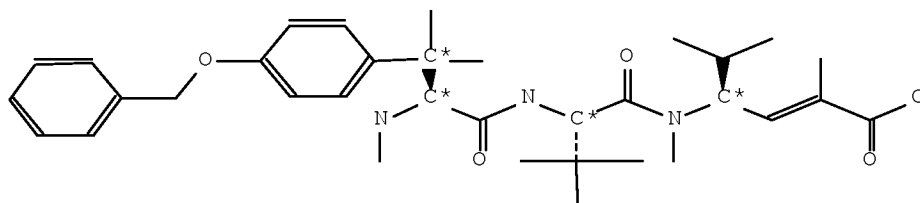
USE - In the treatment of cancers such as solid or non-solid cancers e.g. prostate, breast, colon, bladder, cervical, skin, testicular, kidney, ovarian, stomach, brain, liver, pancreatic or esophageal cancer and lymphoma, leukemia and multiple myeloma (claimed) and proliferative disorders; for preventing restenosis of blood vessels subject to trauma such as angioplasty and stenting.

ADVANTAGE - The compound exhibits favorable therapeutic profile in vivo (e.g. is safe and effective while retaining stability in biological media). The compound is potent tumor growth inhibitor; and inhibits cancer cell growth in vitro and causes tumor regression in vivo. The compound exhibits cytotoxic and/or growth inhibitory effect on cancer cell lines maintained in vitro, exhibits low sensitivity to MDR, low mitotic block reversibility ratio and low cytotoxicity to non-dividing normal cells.

AN.S DCR-798715

CN.S 4-({2-[3-(4-Benzoyloxy-phenyl)-3-methyl-2-methylamino-butyrylamino]-3,3-dimethyl-butyryl}-methyl-amino)-2,5-dimethyl-hex-2-enoic acid

SDCN RAC407



L23 ANSWER 4 OF 5 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
 ACCESSION NUMBER: 2004-390795 [37] WPIX
 DOC. NO. CPI: C2004-146469 [37]
 TITLE: Treating or inhibiting growth of ~~tumor~~ resistant to
~~chemotherapeutic~~ agent comprises administering amide
 compounds
 DERWENT CLASS: B05
 INVENTOR: AYRAL-KALOUSTIAN S; DISCAFANI-MARRO C M; GREENBERGER L M;
 LOGANZO F; ZASK A
 PATENT ASSIGNEE: (AMCY-C) AMERICAN CYANAMID CO
 COUNTRY COUNT: 1

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
CA 2406504	A1	20040320	(200437)*	EN	414	[0]

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
CA 2406504	A1	CA 2002-2406504	20021003

PRIORITY APPLN. INFO: US 2002-666722 20020920

AN 2004-390795 [37] WPIX

AB CA 2406504 A1 UPAB: 20050529

NOVELTY - Treating or inhibiting growth of ~~tumor~~ resistant to at least one
~~chemotherapeutic~~ agent comprises administering amide compounds (I).

DETAILED DESCRIPTION - Treating or inhibiting growth of ~~tumor~~ resistant
 to at least one ~~chemotherapeutic~~ agent comprises administering amide compounds
 of formula R5-C(R3)(R4)-CH(N(R2)(R1))-CO-NH(R6)-CH(R7)-CO- N(R8)R9 (I) or
 their salts.

R1, R2 = H, linear, branched or cyclic saturated or unsaturated group
 containing 1-10C atoms, 0-4 N atoms, 0-4 O atoms and 0-4 S atoms (optionally C
 substituted by =O, =S, OH, OR10, O2CR10, SH, SR10, SOCR10, NH2, NR10H,
 N(R10)2, NHCOR10, NR10COR10, I, Br, Cl, F, CN, CO2H, CHO, COR10, CONH2,
 CONHR10, CON(R10)2, COSH, COSR10, NO2, SO3H, SOR10 or SO2R10, or

NR1R2 = 3-7 membered ring;

R10 = linear, branched or cyclic saturated or unsaturated 1-10C alkyl
 or aryl-R;

R3-R5 = H, linear, branched or cyclic saturated or unsaturated group
 containing 1-10C atoms, 0-4 N atoms, 0-4 O atoms and 0-4 S atoms (optionally C
 substituted by =O, =S, OH, OR10, O2CR10, SH, SOCR10, NH2, NR10H, N(R10)2,
 NHCOR10, NR10COR10, I, Br, Cl, F, CN, CO2H, CO2R10, CHO, COR10, CONH2,
 CONHR10, CON(R10)2, COSH, COSR10, NO2, SO3H, SOR10 or SO2R10), or

CR3R4 = 3-7 membered ring;

R, R6-R8 = H or linear, branched or cyclo saturated or unsaturated
 group containing 1-10C atoms, 0-4 N atoms, 0-4 O atoms and 0-4 S atoms
 (optionally C substituted by =O, =S, OH, OR10, O2CR10, SH, SR10, SOCR10, NH2,
 NR10H, N(R10)2, NHCOR10, NR10COR10, I, Br, Cl, F, CN, CO2H, CO2R10, CHO,
 COR10, CONH2, CONHR10, CON(R10)2, COSH, COSR10, NO2, SO3H, SOR10 or SO2R10;

R9 = Y-CO-Z;

X = OH, OR, =O, =S, O2CR, SH, SR, SOCR, NH2, NHR, N(R)2, NHCOR, NRCOR,
 I, Br, Cl, F, CN, CO2H, CO2R, CHO, COR, CONH2, CONHR, CON(R)2, COSH, COSR,
 NO2, SO3H, SOR or SO2R;

aryl = phenyl, naphthyl, anthracyl, phenanthryl, thienyl, furyl,
 indolyl, pyrrolyl, thiophenyl, benzofuryl, benzothiophenyl, quinolyl,
 isoquinolyl, imidazolyl, thiazolyl, oxazolyl or pyridyl (all optionally
 substituted by R or X);

Y = linear, saturated or unsaturated 1-6C alkyl (optionally substituted by R, aryl-R or X), and
 Z = OH, OR, SH, SR, NH₂, NHR, N(R)₂, NHCH(R₁₁)COOH or NRCH(R₁₁)COOH;
 R₁₁ = R or (CH₂)_nNR₁₂R₁₃;
 n = 1-4;
 R₁₂, R₁₃ = H, R or C(NH)(NH₂);
 provided that when R₅ is an indolyl group of formula (i), then:
 R₁₇ = H or alkyl or acyl (both optionally substituted);
 R₁₈, Q₁-Q₄ = H, halo, alkyl, acyl, OH, alkoxy, acyloxy, NH₂, NH-alkyl, N(alkyl)₂, NH-acyl, NO₂, SH, S-alkyl or S-acyl (where alkyl and acyl are optionally substituted),
 with specified provisos.

Full Definitions are given in the Definitions Field (Full Definitions).

INDEPENDENT CLAIMS are also included for the preparation of compounds of formula (II) by interconversion which comprises treating (II) with ozone in methanol followed by further treatment with dimethylsulfide and reacting the obtained aldehyde compound of formula (III) with a triphenylphosphorane compound of formula (IV) and hydrolyzing with base.

N.B: The provisos do not apply for the above preparation.

ACTIVITY - Cytostatic.

In a test using breast ~~tumor~~ cell line MX-1W, results showed that N-(tert. N-beta,beta-trimethyl-L-phenylalanyl-N1-((1S,2E)-3-carboxy-1-isopropyl-2-butenyl)-N1-dimethyl-3--L-valinamide + 5.0 micro-M 7-(6,7-dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl)-2-(3,4-dimthoxyphenyl)-2- p-tolylsulfenylheptanenitrile (V) exhibited an IC₅₀ value of 1.3 nM, compared to 8.3 nM for ~~paclitaxel~~ + (V).

MECHANISM OF ACTION - ~~Microtubule~~ associated protein associated tubulin polymerization inhibitor.

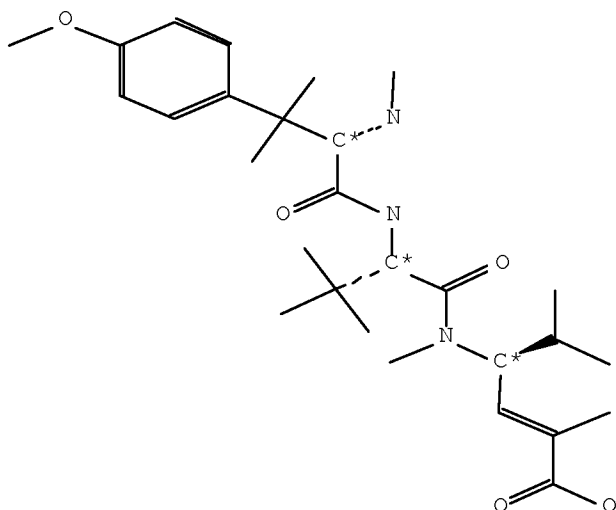
USE - Used for treating or inhibiting growth of ~~tumors~~, particularly of the breast, colon, lung, prostate, melanoma, epidermal, leukemia, kidney, bladder, mouth, larynx, esophagus, stomach, ~~ovary~~, pancreas, liver, skin and brain, ~~tumors~~ which overexpress MDR-1, MXR or MRP and ~~tumors~~ resistant to ~~chemotherapeutic~~ agents, particularly where the resistance is multiple drug resistance (MDR) which is inherent or acquired (all claimed).

AN.S DCR-887301

CN.P HTI-042

CN.S 4-({2-[3-(4-Methoxy-phenyl)-3-methyl-2-methylamino-butyrylamino]-3,3-dimethyl-butyryl}-methyl-amino)-2,5-dimethyl-hex-2-enoic acid

SDCN RADYQO



L23 ANSWER 5 OF 5 WPIX COPYRIGHT 2008 THOMSON REUTERS on STN
 ACCESSION NUMBER: 2003-812505 [76] WPIX
 CROSS REFERENCE: 2005-273356
 DOC. NO. CPI: C2003-225922 [76]
 TITLE: Expanding lumen of a body to eliminate e.g. vascular obstruction involves inserting a stent coated with a composition comprising hemiasterlin derivative into the body
 DERWENT CLASS: B05
 INVENTOR: CAMPAGNA S A; FANG F G; KOWALCZYK J; KOWALCZYK J J; KUZNETSOV G; KUZNETSOV G; SCHILLER S; SELETSKY B M; SPYVEE M; YANG H; GALINA K; HU Y; JAMES K; SHILLER S
 PATENT ASSIGNEE: (EISA-C) EISAI CO LTD; (CAMP-I) CAMPAGNA S A; (FANG-I) FANG F G; (KOWA-I) KOWALCZYK J J; (KUZN-I) KUZNETSOV G; (SCHI-I) SCHILLER S; (SELE-I) SELETSKY B M; (SPYV-I) SPYVEE M; (YANG-I) YANG H; (EISA-C) EISAI R & D MANAGEMENT KK
 COUNTRY COUNT: 102
 PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2003082268	A2	20031009	(200376)*	EN	145	[0]
AU 2003228354	A1	20031013	(200435)	EN		
US 20040229819	A1	20041118	(200477)	EN		
EP 1490054	A2	20041229	(200502)	EN		
KR 2004091748	A	20041028	(200516)	KO		
NO 2004004526	A	20041221	(200520)	NO		
BR 2003008606	A	20050426	(200530)	PT		
MX 2004009209	A1	20050101	(200564)	ES		
JP 2005530717	W	20051013	(200568)	JA	289	
US 20050239870	A1	20051027	(200571)	EN		
CN 1633289	A	20050629	(200574)	ZH		
TW 2004007122	A	20040516	(200628)	ZH		
US 7064211	B2	20060620	(200641)	EN		
US 20060154872	A1	20060713	(200646)	EN		

IN 2004KN01275	P2	20061215	(200723)	EN	
US 7192972	B2	20070320	(200723)	EN	
NZ 535139	A	20070727	(200753)	EN	
JP 2007332160	A	20071227	(200804)	JA	279
US 20080051434	A1	20080228	(200817)	EN	
ZA 2004007611	A	20080227	(200821)	EN	308

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003082268	A2	WO 2003-US8888	20030321
US 20040229819	A1 Provisional	US 2002-366592P	20020322
US 20050239870	A1 Provisional	US 2002-366592P	20020322
US 7064211	B2 Provisional	US 2002-366592P	20020322
US 20060154872	A1 Provisional	US 2002-366592P	20020322
US 7192972	B2 Provisional	US 2002-366592P	20020322
US 20080051434	A1 Provisional	US 2002-366592P	20020322
AU 2003228354	A1	AU 2003-228354	20030321
BR 2003008606	A	BR 2003-8606	20030321
CN 1633289	A	CN 2003-806700	20030321
EP 1490054	A2	EP 2003-726101	20030321
JP 2005530717	W	JP 2003-579806	20030321
JP 2007332160	A Div Ex	JP 2003-579806	20030321
NZ 535139	A	NZ 2003-535139	20030321
US 20040229819	A1 CIP of	WO 2003-US8888	20030321
EP 1490054	A2	WO 2003-US8888	20030321
NO 2004004526	A	WO 2003-US8888	20030321
BR 2003008606	A	WO 2003-US8888	20030321
MX 2004009209	A1	WO 2003-US8888	20030321
JP 2005530717	W	WO 2003-US8888	20030321
US 20050239870	A1	WO 2003-US8888	20030321
US 7064211	B2 CIP of	WO 2003-US8888	20030321
US 20060154872	A1 CIP of	WO 2003-US8888	20030321
US 7192972	B2	WO 2003-US8888	20030321
IN 2004KN01275	P2	WO 2003-US8888	20030321
NZ 535139	A	WO 2003-US8888	20030321
US 20080051434	A1 Cont of	WO 2003-US8888	20030321
TW 2004007122	A	TW 2003-106495	20030324
US 20040229819	A1	US 2003-667864	20030922
US 7064211	B2	US 2003-667864	20030922
US 20060154872	A1 Div Ex	US 2003-667864	20030922
IN 2004KN01275	P2	IN 2004-KN1275	20040901
KR 2004091748	A	KR 2004-714555	20040916
MX 2004009209	A1	MX 2004-9209	20040922
US 20050239870	A1	US 2004-508607	20040922
US 7192972	B2	US 2004-508607	20040922
US 20080051434	A1 Cont of	US 2004-508607	20040922
NO 2004004526	A	NO 2004-4526	20041021
US 20060154872	A1	US 2006-340256	20060126
US 20080051434	A1	US 2007-701969	20070202
JP 2007332160	A	JP 2007-224880	20070830
ZA 2004007611	A	ZA 2004-7611	20040921

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003228354	A1 Based on	WO 2003082268 A
EP 1490054	A2 Based on	WO 2003082268 A

BR 2003008606	A	Based on	WO 2003082268	A
MX 2004009209	A1	Based on	WO 2003082268	A
JP 2005530717	W	Based on	WO 2003082268	A
US 7192972	B2	Based on	WO 2003082268	A
NZ 535139	A	Based on	WO 2003082268	A
US 20080051434	A1	Cont of	US 7192972	B

PRIORITY APPLN. INFO: US 2002-366592P 20020322
 WO 2003-US8888 20030321
 US 2003-667864 20030922
 US 2004-508607 20040922
 US 2006-340256 20060126
 US 2007-701969 20070202

AN 2003-812505 [76] WPIX

CR 2005-273356

AB WO 2003082268 A2 UPAB: 20060203

NOVELTY - Expanding the lumen of a body involves inserting a stent into the body. The stent has a tubular structure and the surface of the structure is coated with a composition comprising hemiasterlin derivative (I).

DETAILED DESCRIPTION - Expanding the lumen of a body involves inserting a stent into the body. The stent has a tubular structure and the surface of the structure is coated with a composition comprising hemiasterlin derivative of formula (I).

n = 0 - 4;

X1, X2 = CRaRb, C(=O) or -SO2-;

Ra, Rb, R3, R4, Rq, R'q = H, (hetero)aliphatic, (hetero)alicyclic or (hetero)aryl;

R1, R2, R5 - R7 = H, -(C=O)Rc, (hetero)aliphatic, (hetero)alicyclic or (hetero)aryl;

Rc = H, OH, ORD, (hetero)aliphatic, (hetero)alicyclic or (hetero)aryl;

R, Rd = (hetero)aliphatic, (hetero)alicyclic or (hetero)aryl;

Q = ORq, SRq, NRq, R'q, N3, =N-OH, (hetero)aliphatic, (hetero)alicyclic or (hetero)aryl;

two of R1 - R7, Rq, R'q = hetero)alicyclic, alicyclic(aryl), heteroalicyclic(aryl), alicyclic(heteroaryl), heteroalicyclic(heteroaryl) or (hetero)aryl; and

provided that when NR7 is linked to R via a double bond, then R7 is absent.

INDEPENDENT CLAIMS are included for the following:

(1) new hemiasterlin derivatives (I) provided that the compound is not a naturally occurring hemiasterlin and the following groups does not occur simultaneously:

(1) n is 1;

(2) X1 and X2 are each C(=O);

(3) R1 is alkyl, acyl, methylene or -CH= bonded to the indole moiety forming a tricyclic moiety (all optionally substituted) or H;

(4) R2 is H, alkyl or acyl (both optionally substituted), or is absent when R1 is -CH=;

(5) R3 is H, or is absent when CR3 and CRyRz are linked by a double bond;

(6) R4 is a group of formula (i);

(7) R5 is H, OH, alkyl or acyl (both optionally substituted);

(8) R6 is H, or alkyl (optionally substituted);

(9) R7 is H or alkyl; and

(10) -R-X2-Q is optionally substituted alkyl moiety, or Q'-C(O)-X; and

(2) a pharmaceutical composition comprising (I), a carrier or diluent and optionally an additional therapeutic agent.

Rw, Ry, Rz = H, alkyl or acyl (both optionally substituted);

Rx = H, an optional substituent or absent;

Y = an optional substituent;

$m = 0 - 4$;
 $Q' = -CH_2-$, $-(CH_2)_2-$, $-(CH_2)_3-$, $-CH_2-CH=CH-$, $-CH_2-C=C-$ or phenylene
 (all optionally substituted);
 $X = -OR'$, $-SR'$ or $NR'R_f$;
 R' , $R_f = H$ or alkyl (optionally substituted); and
 provided that:
 (1) when CR_3 and CR_yR_z are linked by a double bond, then R_z is absent;
 (2) R_y and R_z are not simultaneously H; and
 (3) when R_1 is an optionally substituted methylene or $-CH=$, then R_x is absent.

ACTIVITY - Vasotropic; Cytostatic.

MECHANISM OF ACTION - Smooth Muscle Cell Proliferation Inhibitor; Tumor Growth Regression Inhibitor; Cancer Cell Growth Inhibitor.

The ability of the compounds to inhibit the growth of tumor cell lines was determined. The compounds showed IC_{50} values of 0.1 - 10 nM. Test details are described but no results for specific compounds are given.

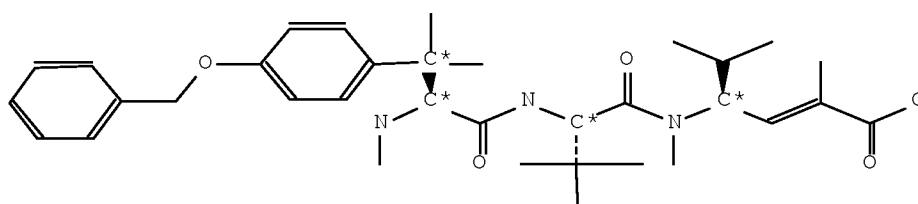
USE - (I) are used for eliminating biliary, gastrointestinal, esophageal, tracheal/bronchial, urethral and/or vascular obstructions; for treating cancer (e.g. prostate, breast, colon, bladder, cervical, skin, testicular, kidney, ovarian, stomach, brain, liver, pancreatic or esophageal cancer or lymphoma, leukemia, multiple myeloma, solid tumor and non-solid tumor); and for preventing or reducing the rate of restenosis (all claimed).

ADVANTAGE - The compounds exhibit cytotoxic and/or growth inhibitor effect on cancer cell lines maintained in vivo or in animal studies using a cancer cell xenograft model; exhibit sensitivity to MDR; exhibit low cytotoxicity to non-dividing normal cells; and/or a favorable therapeutic profile (e.g. safety, efficacy and stability).

AN.S DCR-798715

CN.S 4-({2-[3-(4-Benzoyloxy-phenyl)-3-methyl-2-methylamino-butyrylamino]-3,3-dimethyl-butyryl}-methyl-amino)-2,5-dimethyl-hex-2-enoic acid

SDCN RAC407



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(FILE 'HOME' ENTERED AT 17:20:48 ON 18 JUL 2008)

FILE 'CAPLUS' ENTERED AT 17:21:03 ON 18 JUL 2008

E US2003-666722/APPS

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FILE 'REGISTRY' ENTERED AT 17:21:42 ON 18 JUL 2008

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L3 21 SEA ABB=ON PLU=ON L2 AND ?TETRAMETH?/CNS AND ?VALIN?/CNS AND
 ?TYROS?/CNS AND ?AMID?/CNS
 L4 0 SEA ABB=ON PLU=ON L3 AND ?CARBOX?/CNS AND ?ISOPROP?/CNS AND
 ?BUTEN?/CNS
 L5 0 SEA ABB=ON PLU=ON L3 AND ?ISOPROP?/CNS
 L6 21 SEA ABB=ON PLU=ON L3 AND ?BUTEN?/CNS
 L7 0 SEA ABB=ON PLU=ON L6 AND B/CNS
 L8 12 SEA ABB=ON PLU=ON L6 AND ?CARBOX?/CNS
 L9 1 SEA ABB=ON PLU=ON L8 AND C28H45N3O5/MF
 D

FILE 'REGISTRY' ENTERED AT 17:27:55 ON 18 JUL 2008

L10 STR 676633-18-4
 L11 2 SEA FAM FUL L10

FILE 'CAPLUS' ENTERED AT 17:28:07 ON 18 JUL 2008

L12 2 SEA ABB=ON PLU=ON L11

FILE 'REGISTRY' ENTERED AT 17:28:27 ON 18 JUL 2008

E PACLITAXEL/CN
 L13 1 SEA ABB=ON PLU=ON PACLITAXEL/CN
 D

FILE 'REGISTRY' ENTERED AT 17:28:49 ON 18 JUL 2008

L14 STR 33069-62-4
 L15 170 SEA FAM FUL L14

FILE 'CAPLUS' ENTERED AT 17:28:58 ON 18 JUL 2008

L16 1 SEA ABB=ON PLU=ON L11 AND L15
 L17 270604 SEA ABB=ON PLU=ON ANTITUMOR AGENTS+PFT/CT
 L18 2 SEA ABB=ON PLU=ON L17 AND (L16 OR L12)

FILE 'WPIX' ENTERED AT 17:30:31 ON 18 JUL 2008

L19 0 SEA SSS SAM L10
L20 4 SEA SSS FUL L10
L21 4 SEA ABB=ON PLU=ON L20/DCR
L22 4 SEA ABB=ON PLU=ON L21 AND (?PACLIT? OR ?TUMOR? OR ?TUMOUR?
OR ?CHEMOTHER? OR ?MICROTUB? OR ?OVAR?)

FILE 'CAPLUS' ENTERED AT 17:32:42 ON 18 JUL 2008

D QUE L12

FILE 'WPIX' ENTERED AT 17:32:48 ON 18 JUL 2008

D QUE L22

FILE 'CAPLUS, WPIX' ENTERED AT 17:32:53 ON 18 JUL 2008

L23 5 DUP REM L12 L22 (1 DUPLICATE REMOVED)
ANSWERS '1-2' FROM FILE CAPLUS
ANSWERS '3-5' FROM FILE WPIX
D L23 IBIB ABS HITIND HITSTR 1-2
D L23 IBIB ABS HITSTR 3-5